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Smoking, Air Pollution, and the High Rates of Lung Cancer in Shenyang, China

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A case-control study involving interviews with 1,249 patients with lung cancer and 1,345 population-based controls was conducted in Shenyang, an industrial city in northeastern China, where mortality rates are high among men and women. Cigarette smoking was found to be the principal cause of lung cancer in this population, accounting for 55% of the lung cancers in males and 37% in females. The attributable risk percentage among females is high compared to elsewhere in China, largely because of a higher prevalence of smoking among women. After adjustment for smoking, there were also significant increases in lung cancer risk associated with several measures of exposure to air pollutants. Risks were twice as high among those who reported smoky outdoor environments, and increased in proportion to years of sleeping on beds heated by coal-burning stoves (kang), and to an overall index of indoor air pollution. Threefold increases in lung cancer risk were found among men who worked in the nonferrous smelting industry, where heavy exposures to inorganic arsenic have been reported. The associations with both smoking and indoor air pollution were stronger for squamous cell and small cell carcinomas than for adenocarcinoma of the lung. Risks due to smoking or air pollution were not greatly altered by adjustment for consumption of fresh vegetables or sources of beta carotene or retinol, prior chronic lung diseases, or education level. The findings suggest that smoking and environmental pollution combine to account for the elevated rates of lung cancer

mortality in Shenyang. [*J Natl Cancer Inst* 81:1800-1806, 1989]

A distinctive geographic gradient for lung cancer mortality exists in China, particularly among females (1,2). Mortality rates are elevated in northern provinces, with the highest rates occurring in both sexes in Liaoning. The exceptionally high rates among Liaoning women result in a male-to-female ratio in lung cancer mortality of 1:6, one of the lowest in the world (3). A correlation study linking lung cancer death rates and measures of industrial activity in 10 cities of Liaoning suggested that, even after smoking was taken into account, atmospheric pollution may contribute to lung cancer risk (4). To evaluate determinants of the elevated mortality and to test hypotheses regarding pollutant exposure as a risk factor for

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lung cancer, we conducted a case-control study in Shenyang, the industrial capital of Liaoning.

Methods

Subjects

During the period from September 1985 to September 1987, all newly diagnosed cases of primary lung cancer (9th revision, ICD 162) among residents of urban Shenyang aged 30-69 years were sought for enrollment in the study. Patients were identified by a rapid cancer reporting and referral system established for this study. The system involved all of the area hospitals, each of which reported to the Shenyang Cancer Registry. All diagnoses and histologic or cytologic slides of cases were reviewed by a special study group that met weekly through the study period. The group included pulmonary disease physicians (five) and senior pathologists (four).

Population-based controls, frequency-matched to the expected (based on earlier cancer registry data) age and sex distribution of the cases, were selected from the Shenyang urban area by a three-stage stratified random sampling scheme. The initial unit for randomization was the neighborhood committee—a geographic area defined by the municipal government. To select a control in a particular sex and 5-year age category, a neighborhood committee was sampled with replacement, weighting by its population, from among the 1,404 in Shenyang. Then, a household group within the committee was randomly chosen. Each committee typically encompasses 10-25 household groups and represents about 100 persons. In the final stage, among all persons in the specific sex and age category within the household group, one person was randomly selected.

Data Collection and Coding

Personal interviews with the subjects were conducted in the subject's home, the hospital-clinic, or the work site. The interviewers were experienced nurses aged 45-55 years who were employed and trained for this study. All interviews were recorded on cassettes for later review by a field supervisor. A structured, precoded questionnaire inquired about demographic characteristics, residential and occupational histories, smoking, diet (inquiring about the frequency of consumption, approximately 5 yr prior to interview, of 33 commonly eaten food items) and cooking practices, prior pulmonary conditions, and family history of cancer. Smokers were defined as those who had ever smoked cigarettes (commercial or handrolled) for 6 months or longer. Detailed information was obtained on potential exposure to indoor and outdoor air pollution, including information on housing and environmental conditions of every residence in which a subject lived for 3 or more years.

The information collected was edited and coded in Shenyang and computerized in the United States. Industry and occupation titles were coded according to the system used in the 1982 Population Census of the People's Republic of China. Locations of all Shenyang residences were coded

on the basis of their distance and direction from the Shenyang smelter, a major point source of pollution in the city.

Several indices of pollution were created by averaging responses across residences, weighting according to years lived at each. One index represented an average response to the subjective question, "Within a 100-m radius of your residence, how smoky was the outdoor environment? Was it very smoky, somewhat smoky, slightly smoky, or not smoky at all?" Similarly coded variables represented perceived smokiness indoors during the winter and summer. In addition, more objective measures were based on the types of fuels used and location within the home where heating and cooking were carried out. In particular, use of kang was ascertained for each residence. Kang are brick beds under which heated smoke from coal, wood, grass, or other kinds of fuel is passed through pipes before venting to the outside through openings in the sides of the residence. Occasionally, the fuel is burned directly under the bed, which we have designated as "burning kang." In Shenyang and in rural Liaoning, kang are used from October through March to protect against the cold Manchurian winter. For each individual, we evaluated the number of years kang was used, plus the total years of sleeping on kang with fuel burned under the bed. We also calculated an overall indoor air pollution index, P , defined as:

$$P = \sum Y_i (a_i + b_i + c_i) / \sum Y_i$$

where Y_i = years lived at each residence i ; a_i = 0 if central heat used and 1 otherwise (predominantly coal heat); b_i = 0 if the cooking fuel all year was gas, $\frac{1}{2}$ if the cooking fuel in summer only was gas, and 1 otherwise (predominantly coal used all yr); c_i = 0 if the cooking place was in a separate kitchen, $\frac{1}{2}$ if the cooking place was in a bedroom or entry corridor in winter, and 1 if the cooking place was in a bedroom or entry corridor all year. Summation was across all residences. The definitions of a_i and b_i were changed slightly if the residence was a rural one, where central heat and gas were rarely used. For rural residences, a_i = 1 if the heating system was based on burning kang and 0 otherwise (predominantly kang, but fuel not burned directly under the bed); b_i = 1 if the cooking fuel was coal and 0 otherwise (usually dry kindling).

Thus, the index P for each person assumed a value from 0 to 3, with values below 1 indicating potential for relatively low lifetime exposure to indoor air pollution from burning coal.

Food group variables were formed by summing the yearly consumption frequencies of the constituent food items after adjusting for length of season. An index of vitamin A was created by assigning each food item a weight equivalent to its nutrient density (IU of vitamin A/100 g) (5).

Statistical Methods

The statistical analyses were based on multivariate techniques for case-control data (6). Logistic regression analyses were used to estimate summary relative risks (RRs) of lung cancer associated with various factors while adjusting for other factors. The regression models generally contained terms for age, education (no formal education,

primary or middle school, or high school and higher), smoking (nonsmoker, light, moderate, or heavy smoker), and the indoor air pollution index. We also made additional adjustments for prior history of tuberculosis (yes or no) or chronic bronchitis (yes or no), ever employed in the nonferrous smelting industry (yes or no), the percentage of the subject's life spent in urban areas, and for level of consumption of vitamin A, protein, and other dietary variables. However, these variables had very little effect on the estimates of risks associated with smoking or pollution. Interactions between smoking and pollution indices were evaluated by adding appropriate cross-product terms to the models, with multiple degree-of-freedom significance tested by contrasting likelihoods with and without the cross-product terms included. The regression analyses were run separately for males and females, and also repeated separately for squamous cell or oat cell cancer and adenocarcinoma. Finally, we calculated estimates of population attributable risks (PARs), and associated 95% confidence intervals (CI) as measures of the percentages of lung cancers due to smoking and air pollution (7).

Results

Interviews were completed with 1,249 cancer patients and 1,345 controls. An additional 69 incident lung cancer cases were identified, but 60 had died or were too ill to be interviewed, seven could not be found, and two refused interview, so that the case participation rate was 95%. There were also 64 patients with suspected lung cancer who were excluded from the study when cancer was ruled out by further diagnostic workup. Three eligible controls refused the interview.

The sex and age distributions of the cases and controls were similar (table 1). Fifty-eight percent of the participants were male, with a median age of 59 among males and 56 among females. Most men had at least a primary or middle school education, whereas nearly 50% of the women had no formal education. Among both males and females, the cases tended to be slightly less educated than the controls.

The diagnosis of lung cancer was based on histologic evidence for 83% of the male and 73% of the female cases (table 2). Squamous cell carcinomas accounted for about

Table 2. Percentage distribution of cases by histologic diagnosis and diagnostic method

| | Male | Female |
|-----------------------------|--------------|--------------|
| Histologic diagnosis | | |
| Squamous cell carcinoma | 42.2 (50.7)* | 22.9 (31.5)* |
| Adenocarcinoma | 22.3 (26.8) | 27.9 (38.4) |
| Oat cell carcinoma | 12.1 (14.5) | 12.5 (17.2) |
| Large cell carcinoma | 1.1 (1.3) | 1.2 (1.7) |
| Others | 5.4 (6.5) | 8.3 (11.4) |
| Unknown | 16.8 | 27.3 |
| Diagnostic method | | |
| Pathology | 58.4 | 42.6 |
| Cytology | 26.7 | 32.4 |
| X ray/clinical | 14.9 | 25.0 |

*Percentage after excluding those with unknown cell type.

50% of the histologically diagnosed cases among men and about 33% among women. Adenocarcinoma was the major cell type among females (38%), compared to 27% among males. Anaplastic small cell (oat cell) carcinomas accounted for 15% of the tumors among males and 17% among females.

Tobacco smoking was reported by 86% of the male and 55% of the female patients. The corresponding percentages among controls (70% and 35%) were significantly lower. Overall, smoking was associated with a 2.7-fold [95% confidence interval (CI) = 2.1-3.5] increase in lung cancer among males, and a 2.6-fold (95% CI = 2.0-3.3) increase among females after adjusting for age and education. Among smokers, the median numbers of cigarettes usually smoked per day were 19 and seven for males and females, respectively, and almost all (92%) were current or recent (within the past 5 yr) smokers. For both sexes, the RRs of lung cancer tended to rise with increasing numbers of cigarettes smoked per day and with duration of smoking (table 3). The trends were

Table 3. RRs of lung cancer by cell type associated with intensity and duration of smoking*

| Histologic type | Cigarettes/day | Duration of smoking (yr) | | |
|----------------------------------|----------------|--------------------------|-------------------|------|
| | | 1-29 | 30-39 | 40+ |
| <i>Males</i> | | | | |
| All lung cancer | 1-19 | 1.8 | 2.1 | 3.3 |
| | 20-29 | 1.5 | 2.7 | 6.0 |
| | 30+ | 5.3 | 4.9 | 17.1 |
| Squamous cell/oat cell carcinoma | 1-19 | 2.3 | 2.9 | 5.0 |
| | 20-29 | 2.6 | 3.9 | 10.4 |
| | 30+ | 7.7 | 8.3 | 31.2 |
| Adenocarcinoma | 1-19 | 1.4 ^{ns} | 2.2 | 2.6 |
| | 20-29 | 0.7 ^{ns} | 1.5 ^{ns} | 3.6 |
| | 30+ | 5.4 | 3.2 | 11.8 |
| <i>Females</i> | | | | |
| All lung cancer | 1-19 | 1.4 ^{ns} | 3.1 | 3.4 |
| | 20+ | 2.1 ^{ns} | 3.4 | 9.4 |
| Squamous cell/oat cell carcinoma | 1-19 | 1.8 | 4.2 | 5.3 |
| | 20+ | 2.5 ^{ns} | 2.4 ^{ns} | 19.9 |
| Adenocarcinoma | 1-19 | 0.9 ^{ns} | 2.2 | 1.9 |
| | 20+ | — | 3.7 | 6.8 |

*All risks relative to those for nonsmokers and adjusted for age and education. All RRs were statistically significantly ($P < .05$) elevated except as noted by "ns" (not significant).

Table 1. Percentage distribution of cases and controls by age and education

| | Male | | Female | |
|-------------------------------------|-------------------|----------------------|-------------------|----------------------|
| | Case (n = 729) | Control (n = 788) | Case (n = 520) | Control (n = 557) |
| Age | | | | |
| 30-44 | 7.4 | 7.4 | 7.5 | 8.8 |
| 45-54 | 20.2 | 25.1 | 28.9 | 28.7 |
| 55-59 | 26.1 | 22.1 | 28.7 | 27.1 |
| 60-64 | 26.6 | 24.4 | 21.2 | 21.0 |
| 65-69 | 19.8 | 21.1 | 13.9 | 14.4 |
| Education | | | | |
| No formal education | 19.2 | 15.1 | 51.4 | 43.8 |
| Primary and junior middle school | 65.2 | 65.8 | 42.1 | 45.6 |
| High school and technical institute | 9.6 | 11.3 | 5.0 | 6.0 |
| University | 5.7 | 7.7 | 1.3 | 2.1 |

Table 4. RRs of lung cancer according to home heating and cooking characteristics*

| | No. of yr of use | Male | | | Female | | |
|--|---------------------|------|---------|------|--------|---------|------|
| | | Case | Control | RR | Case | Control | RR |
| Heating method | | | | | | | |
| Kang (coal) | 0 | 16 | 20 | 1.0 | 4 | 17 | 1.0 |
| | 1-39 | 266 | 336 | 0.8 | 164 | 201 | 2.4 |
| | 40-49 | 138 | 135 | 0.9 | 65 | 92 | 1.9 |
| | 50+ | 307 | 297 | 1.0 | 287 | 246 | 3.4† |
| Burning kang | 0 | 556 | 667 | 1.0 | 415 | 484 | 1.0 |
| | 1-19 | 91 | 68 | 1.7† | 40 | 38 | 1.3 |
| | 20+ | 82 | 53 | 2.1† | 65 | 35 | 2.3† |
| Single standing coal stove | 0 | 60 | 68 | 1.0 | 49 | 55 | 1.0 |
| | 1-39 | 440 | 510 | 0.8 | 331 | 374 | 0.9 |
| | 40-49 | 140 | 127 | 1.0 | 72 | 73 | 0.9 |
| | 50+ | 84 | 80 | 1.0 | 66 | 53 | 1.2 |
| Coal stove with pipes extending to other rooms | 0 | 559 | 642 | 1.0 | 401 | 465 | 1.0 |
| | 1-19 | 119 | 121 | 1.1 | 81 | 68 | 1.4 |
| | 20+ | 48 | 20 | 2.3† | 35 | 24 | 1.5 |
| Central heating (gas) | 0 | 337 | 370 | 1.0 | 312 | 284 | 1.0 |
| | 1-9 | 125 | 110 | 1.1 | 68 | 84 | 0.8 |
| | 10-29 | 142 | 192 | 0.7 | 85 | 117 | 0.7 |
| | 30+ | 85 | 115 | 0.8 | 54 | 69 | 0.8 |
| Cooking method and location | | | | | | | |
| Gas fuel | 0 | 403 | 396 | 1.0 | 304 | 295 | 1.0 |
| | 1-9 | 138 | 159 | 0.9 | 99 | 113 | 0.9 |
| | 10+ | 188 | 233 | 0.8 | 117 | 149 | 0.8 |
| Cooking place in bedroom | 0 | 570 | 678 | 1.0 | 435 | 503 | 1.0 |
| | 1-29 | 75 | 64 | 1.2 | 34 | 25 | 1.5 |
| | 30+ | 84 | 46 | 2.1† | 51 | 29 | 1.8† |

* All RRs adjusted for age, education, and smoking.

† P < .05.

stronger for squamous cell and oat cell carcinomas than for adenocarcinoma, with 31-fold (males) and 20-fold (females) excesses of squamous cell and oat cell cancers in long-term heavy smokers. Risks of lung cancer associated with smoking were not modified by diet. Furthermore, no protective effects for retinol and carotene-containing foods were found among smokers or nonsmokers of either sex.

On average, the cases had lived in 3.6 different residences over their lifetimes and the controls in 3.7 (both figures exclude places lived in for <3 yr). The cases spent 62% and the controls 59% of their lifetimes in urban areas. About 75% of all residences were single-story houses.

Table 4 presents risks of lung cancer according to duration of exposure to several types of residential heating and cooking. Nearly all subjects reported having kang in at least one of their homes. Trends in risk with years of living in a house with kang were seen only among females; all RRs were elevated, although only a small number of nonusers of kang were in the baseline reference category. The RRs rose among both sexes; however, when classified by duration of use of burning kang, the RRs reached 1.9 among males and 2.2 among females who reported sleeping on kang with fuel burned directly below the bed for more than 20 years. Risks declined with increasing use of gas (and consequently decreasing use of coal) for both heating and cooking. Risks were also higher when cooking took place in the bedroom or entry corridor to the bedroom than in a separate kitchen or elsewhere in the house.

Table 5 shows the risks associated with ordered categories of the overall indoor air pollution index, P, defined earlier.

The RRs tended to rise with increasing indoor air pollution exposure among both males and females. Smoking-adjusted excess risks of 50% or more were reported among the most heavily exposed cases and controls. As shown in table 5, the trends in risk were even more pronounced for squamous cell or oat cell carcinomas. The trends shown in tables 4 and 5 were generally similar in nonsmokers and smokers.

Although most persons reported that their environments were not smoky, more cases than controls reported smoky indoor and outdoor environments (table 6). Compared to groups who reported no smoky environment, twofold increases in lung cancer risk were seen among those who said their neighborhoods were smoky. The excess risks were seen for both squamous cell or oat cell cancers and adenocarcinoma.

Thirty-four percent of the men and 27% of the women in this study reported a factory within 200 m of at least one of their residences (table 7). Based on industrial codes used by the 1982 Chinese Census, we classified the factories into one of 10 specific categories. More cases than controls reported living in a residence within 200 m of any type of factory. Analysis by type of factory revealed that only those living near ferrous or nonferrous metallurgic industries showed significantly elevated risks for both males and females, even after controlling for their years of working in those factories (data not shown). The RRs rose with increased years of living near such factories; RRs reached 2.7 (95% CI = 1.1-6.5) for males and 3.2 (95% CI = 1.0-10.5) for females who lived near the factories for more than 20 years.

We also compared the residential proximity of cases and

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Table 5. RRs of lung cancer according to average indoor air pollution exposure*

| Air pollution index, P | Case | Control | All cell types | | Squamous cell/oat cell carcinoma | | Adenocarcinoma | |
|------------------------|------|---------|----------------|---------|----------------------------------|---------|----------------|---------|
| | | | RR | 95% CI | RR | 95% CI | RR | 95% CI |
| Males | | | | | | | | |
| 0-9 | 209 | 264 | 1.0 | — | 1.0 | — | 1.0 | — |
| 1.0-1.4 | 258 | 294 | 1.1 | 0.8-1.4 | 1.3 | 0.9-1.7 | 1.1 | 0.7-1.6 |
| 1.5-1.9 | 168 | 163 | 1.2 | 0.9-1.6 | 1.5 | 1.0-2.0 | 1.0 | 0.6-1.9 |
| 2.0+ | 94 | 67 | 1.6 | 1.1-2.3 | 1.9 | 1.0-2.6 | 1.5 | 0.9-2.8 |
| Females | | | | | | | | |
| 0-9 | 171 | 217 | 1.0 | — | 1.0 | — | 1.0 | — |
| 1.0-1.4 | 183 | 193 | 1.2 | 0.9-1.6 | 1.1 | 0.7-1.7 | 1.2 | 0.8-1.9 |
| 1.5-1.9 | 110 | 104 | 1.3 | 0.9-1.9 | 1.2 | 0.7-2.0 | 1.5 | 0.9-2.4 |
| 2.0+ | 56 | 43 | 1.5 | 1.0-2.4 | 2.0 | 1.1-3.6 | 1.0 | 0.5-2.2 |

*All RRs adjusted for age, education, and smoking.

Table 6. RRs of lung cancer associated with perceived smokiness

| | Male | | | | Female | | | |
|--|------|---------|------|---------|--------|---------|------|---------|
| | Case | Control | RR | 95% CI | Case | Control | RR | 95% CI |
| Indoor smoke from heating (in winter): | | | | | | | | |
| Not smoky | 282 | 350 | 1.0* | — | 258 | 329 | 1.0* | — |
| Somewhat/slightly smoky | 249 | 259 | 1.2 | 1.0-1.5 | 146 | 154 | 1.2 | 0.9-1.6 |
| Smoky | 198 | 179 | 1.3 | 1.0-1.7 | 116 | 74 | 2.0 | 1.4-2.8 |
| Smoke of outdoor environment | | | | | | | | |
| Not smoky | 276 | 422 | 1.0† | — | 241 | 342 | 1.0† | — |
| Somewhat/slightly smoky | 190 | 190 | 1.5 | 1.2-2.0 | 118 | 121 | 1.4 | 1.1-2.0 |
| Smoky | 262 | 176 | 2.3 | 1.7-2.9 | 161 | 94 | 2.5 | 1.8-3.5 |

*All RRs adjusted for age, education, and smoking.

†RRs also adjusted for indoor air pollution index P.

Table 7. RRs of lung cancer associated with duration of living within 200 m of industrial factories*

| Industrial category of factory | Duration of living (yr) | | | Percentage of persons reporting factory within 200 m |
|-----------------------------------|----------------------------|------|------|--|
| | 0 | 1-19 | 20+ | |
| <i>Males</i> | | | | |
| Any | 1.0 | 1.3 | 1.7† | 33.6 |
| Electricity, gas production | 1.0 | 0.7 | 1.7 | 1.6 |
| Food, tobacco production | 1.0 | 2.4 | 2.3 | 4.1 |
| Textiles | 1.0 | 1.1 | 2.4 | 2.4 |
| Wood, paper | 1.0 | 0.5 | 1.8 | 2.4 |
| Chemical, rubber, drug | 1.0 | 1.5 | 2.2† | 7.9 |
| Cement, glass, asbestos | 1.0 | 3.6† | 3.5† | 3.0 |
| Ferrous, nonferrous smelter | 1.0 | 1.5 | 2.7† | 4.3 |
| Metal products | 1.0 | 1.2 | 0.8 | 6.2 |
| Machinery | 1.0 | 1.2 | 1.3 | 17.1 |
| Restaurants | 1.0 | 1.7 | 2.2 | 1.8 |
| <i>Females</i> | | | | |
| Any | 1.0 | 1.8† | 1.6† | 26.5 |
| Electricity, gas production | 1.0 | — | — | 0.6 |
| Food, tobacco production | 1.0 | 0.9 | 0.7 | 2.6 |
| Textiles | 1.0 | 2.2 | 0.5 | 1.8 |
| Wood, paper | 1.0 | 0.6 | 9.6† | 1.7 |
| Chemical, rubber, drug | 1.0 | 2.0 | 0.9 | 6.1 |
| Cement, glass, asbestos | 1.0 | 2.1 | 1.0 | 2.3 |
| Ferrous, nonferrous smelter | 1.0 | 1.9 | 3.2† | 3.5 |
| Metal products | 1.0 | 4.4† | 2.8 | 4.2 |
| Machinery | 1.0 | 1.9† | 1.2 | 12.5 |
| Restaurants | 1.0 | 4.1 | 2.8 | 1.8 |

*All RRs adjusted for age, education, smoking, and indoor air pollution index P.

†P < .05.

controls to the Shenyang nonferrous smelter using street addresses to classify distance. There was an excess of male cases who had lived within 1 km of this particular factory (table 8). The RR associated with having a residence near the smelter was 3.0 (95% CI = 1.5-6.0) after controlling for smoking and working experience in the factory. No excess risk was seen in females or persons of either sex who lived more than 1 km beyond the smelter.

From employment histories recorded during the interviews, the cases and controls had generally similar distributions of work in major industrial and occupational categories, although fewer male cases were ever employed as profes-

Table 8. RRs of lung cancer according to distance of closest residence to the Shenyang smelter

| Distance (km) | Case | Control | RR | 95% CI |
|----------------|------|---------|------|---------|
| Males | | | | |
| <1 | 35 | 12 | 3.0* | 1.5-6.0 |
| 1.0-1.9 | 63 | 79 | 0.9 | 0.6-1.3 |
| 2.0-2.9 | 148 | 169 | 0.9 | 0.7-1.2 |
| 3.0+ | 483 | 525 | 1.0 | — |
| Females | | | | |
| <1 | 11 | 10 | 1.0* | 0.4-2.5 |
| 1.0-1.9 | 35 | 52 | 0.6 | 0.4-1.0 |
| 2.0-2.9 | 94 | 105 | 0.9 | 0.6-1.3 |
| 3.0+ | 380 | 390 | 1.0 | — |

*All RRs adjusted for age, education, smoking, and indoor air pollution index P, and relative to risks for those living 3+ km from the smelter.

Table 9. PAR percentages of lung cancer associated with cigarette smoking and indoor air pollution exposure

| Index | All types of lung cancer | | Squamous cell/oat cell carcinoma | | Adenocarcinoma | |
|---------------------------------|--------------------------|--------|----------------------------------|--------|----------------|---------|
| | PAR | 95% CI | PAR | 95% CI | PAR | 95% CI |
| Males | | | | | | |
| Smoking* | 55 | 46-65 | 69 | 59, 79 | 38 | 17, 59 |
| Air pollution† (Index > 1.0) | 13 | -1, 27 | 18 | 2, 34 | 7 | -16, 31 |
| Females | | | | | | |
| Smoking* | 37 | 29, 44 | 46 | 34, 57 | 17 | 4, 31 |
| Air pollution | 17 | 3, 30 | 16 | -4, 35 | 12 | -10, 34 |

*PAR of lung cancer associated with smoking after adjusting for air pollution.

†PAR of lung cancer associated with air pollution after adjusting for smoking.

sional or white collar workers. Employment in the nonferrous metal smelting and refining industry (a specific 3-digit manufacturing code) was associated with a smoking-adjusted increased risk of lung cancer among males (RR = 3.6; 95% CI = 1.6-8.2). A total of 26 cases and eight controls were smelter workers. These small numbers hindered evaluation of trends by duration or timing of employment, but most of these men had worked in the smelting industry at least 20 years. Among females, seven cases and five controls (RR = 1.3; 95% CI = 0.4-4.4) had worked in the smelter.

To assess the relative proportions of lung cancers associated with cigarette smoking, air pollution, and occupation in Shenyang, we calculated estimates of PAR. Because only a small number of workers were in the nonferrous smelting industry, less than 4% of the cases among males and 1% among females could be attributed to occupational exposures in smelters. Table 9 lists the PARs associated with smoking and air pollution, using values of the indoor air pollution index, *P*, less than 1.0 to categorize "nonexposed" and values equal to or greater than 1.0 to categorize "exposed" individuals. As shown, smoking is the dominant cause of lung cancer, accounting for 55% (95% CI = 45%-65%) of the cases among men and 37% (95% CI = 29%-44%) among women. The percentages of squamous cell or oat cell cancers due to smoking were higher, 69% and 46%, respectively, among males and females, than the percentages of adenocarcinoma due to smoking (38% among males and 17% among females). Contributions from air pollution were less, but 13% (-1%-27%) and 17% (3%-30%) of the cases among men and women were associated with high exposure to indoor air pollution.

Discussion

This large population-based case-control study revealed that tobacco smoking is the dominant cause of lung cancer in an area of China where rates are exceptionally high. There were clear trends of increasing risk of lung cancer with rising cigarette consumption, with more than a 25-fold increase in squamous cell or oat cell cancers among heavy smokers.

While not surprising to western observers, the findings, when coupled with similar results in Shanghai (8), should remove all doubt of whether smoking Chinese cigarettes is harmful. This notion that Chinese cigarettes are not harmful was prevalent throughout China and even among many health professionals at the start of this study. Smoking also appears to account for at least part of the geographic gradient in lung cancer mortality in China, where high rates among females cluster in the northern provinces (2). Among women in our control series, 35% had smoked cigarettes, a figure nearly double that reported among females of similar age in Shanghai and elsewhere in China (8,9). We did not observe expected protective effects for frequent consumption of either beta-carotene or retinol, and risks associated with smoking did not vary with diet.

The primary contribution of this study, however, may be its ability to examine risks of lung cancer associated with pollution from industrial and domestic sources. Shenyang is anecdotally said to have among the highest levels of air pollution in the world, even though there are fewer automobiles than in western cities. Pollution results mainly from industrial emissions and from combustion of fuel (mostly coal) for home heating and cooking. Shenyang is a densely populated city (2,700,000 persons in 164 km²), with most people traditionally living in close quarters in single-story dwellings heated by kang. We measured wintertime benzo(a)pyrene concentrations in and around 10 single-story homes, 10 two-story homes, and 10 apartment buildings three or more stories tall. There was little variation in outdoor levels by housing type. Average concentration was around 60 ng/m³ in January, a level 60 times higher than the recommended upper limit for U.S. urban air (10). Inside, however, average levels differed according to structure. The level was highest (and exceeded outdoor levels) for traditional single-story homes, declined slightly in two-story homes, and dropped by more than 50% in high-rise apartment buildings.

We found significant associations between lung cancer risk and measures of indoor air pollution, despite the relative crudeness of the pollution indices used and the likely misclassification of exposure that would have dampened RR estimates. Risks were 50%-70% higher among those who spent most of their lives living in homes heated by coal and using coal as the primary cooking fuel. Although most homes had kang, persons who slept on kang in which fuel was directly burned, and those who cooked in their sleeping quarters, had higher risks of lung cancer than those who did not. These measures of pollution were created from responses to questions that should be objectively answered (i.e., questions on types of heating and cooking facilities), and risk patterns based on these measures correlated well with patterns derived from subjective appraisals of house and neighborhood smokiness. It is noteworthy that the effects of indoor air pollution were stronger for squamous cell and oat cell cancers than for adenocarcinoma, thus paralleling the effects of cigarette smoking.

The link between coal burning and lung cancer in Shenyang is qualitatively similar to that observed in a high-risk area of Yunnan province in south China, where living in houses without chimneys that are heated by soft lo-

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cal coal was found to contribute more than cigarette smoking to the elevated rates of lung cancer in women (11). In western countries, the effects of air pollution on lung cancer risk have been more difficult to identify and disentangle from the effects of smoking and occupational exposure (10-12). In Shenyang, the high levels of air pollution provide a wider range of exposure over which to evaluate dose-response trends with lung cancer, after adjustment for smoking and other risk factors. Our conclusion is that the concentrated use of coal-burning stoves in Shenyang is a likely cause of lung cancer in the area, and perhaps 10%-20% of the cases are related to pollution.

This study also evaluated risks associated with a particular point source of pollution, i.e., the Shenyang smelter, which has released inorganic arsenic and other metals. Workers in the nonferrous smelting industry were found to have a three-fold increased risk of lung cancer, similar to workers who are exposed to inorganic arsenic in U.S. copper smelters (13,14). We plotted residences according to distance from the smelter's central stacks and found more cases than controls among men living within 1 km. The resultant excess risk among males was not accounted for by employment in the industry or smoking. As part of the investigation, we obtained soil samples at varying distances from the smelter. Assays of metals, including inorganic arsenic, revealed a rapid drop as distance from the smelter increased; the highest levels were within 1 km. Thus, similar to other areas of the world (15-18), particulate smelter emissions in Shenyang have been detected in the surrounding neighborhood. However, the excess risk of lung cancer among those who lived near the smelter was observed in males but not in females. Therefore, we cannot definitively confirm reports of higher lung cancer risk among residents living in the vicinity of smelters in the United States and Sweden (18-21), despite the large numbers of persons living within a few kilometers of the Shenyang smelter.

A recently completed investigation of lung cancer in Shanghai suggested that another form of indoor pollution, namely, prolonged exposure to oil volatiles from cooking with a wok at high temperature, may be related to increased risk of both squamous cell carcinoma and adenocarcinoma of the lung (22). Risks among Shanghai women rose with the frequency of wok cooking, with reported smokiness of the house, and with reported eye irritation during cooking. The risks were most pronounced when exposure to rapeseed oil fumes was involved. Although we also found similar trends for some of these variables, we could not adequately examine these hypotheses, because our questionnaire did not include an extensive cooking method section and rapeseed oil was rarely used in Shenyang. Conversely, the Shanghai study could not evaluate lung cancer risks from kang or other heating exposure, since less than 5% of the homes in Shanghai were heated.

In summary, this large population-based case-control study has confirmed that cigarette smoking is the major determinant of lung cancer in Shenyang, as it is elsewhere in the world. High levels of indoor air pollution from coal-burning stoves also appear to contribute, and they combine with an elevated frequency of smoking to account for the high rates of lung cancer among women in northeast China.

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